

### **Remarks**

Reconsideration of the application is respectfully requested in view of the foregoing amendments and following remarks. Claims 1-21 and 23-30 are pending. Claim 22 is canceled. Claims 1-30 are rejected. Claims 1, 8, 11-13, 18, 19 and 26 are amended herein.

### ***Interview Summary***

Applicant thanks the Examiner for his time during a telephonic interview on December 4, 2007. Features of claims 1 and 13 and U.S. Patent No. 6,503,720 to Wittwer et al. (Wittwer) were discussed.

In light of proposed language, the Examiner cited to Wittwer at col. 5, line 60, to col. 6, line 10, as possibly forming a rejection for claim 1. After reviewing the cited section of Wittwer, Applicant finds sufficient language in the claim to distinguish over Wittwer.

In the above-indicated section, Wittwer does describe “vertical window parameters. . . defined as  $a/n/b$ , wherein  $a$  is the number of points taken from the left,  $n$  is the order of the polynomial and  $b$  is the number of points taken from the right.” As understood by Applicant, the passage does not describe “a first endpoint and an other endpoint of the usable portion of the standard sigmoid curve [determined] via a second derivative of the standard sigmoid curve” because the window parameters are not determined via a second derivative.

The Examiner cited to Wittwer at col. 5, line 60, to col. 6, line 10, and Wittwer at col. 12 lines 8-13, as possibly forming a rejection for claim 13. After reviewing the cited sections of Wittwer, Applicant finds sufficient language in the claim to distinguish over Wittwer.

In the latter of the above-indicated sections, Wittwer does describe calculating “a fractional cycle number of the control sample ( $T$ ).” As understood by Application, the passage does not describe “calculating the concentration of the substance in the test sample based on a subset of observations of the test sample, wherein the subset is within the range of observational values indicated by the usable portion of the sigmoid curve.”

***Rejections under 35 U.S.C. § 103(a) in view of Wittwer***

The Action rejects claims 1-6, 8-11, 13-22 and 24-30 under 35 U.S.C. § 103(a) as being unpatentable in view of U.S. Patent No. 6,503,720 to Wittwer et al. (Wittwer). Applicant respectfully traverses this rejection.

***Amended independent claim 1 and dependent claims 2-6 are allowable over Wittwer***

Amended claim 1 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to calculate concentration of a substance in a test sample, the method comprising:

for at least one observation of a metric for the test sample, finding where on a usable portion of a standard sigmoid curve the observation lies, wherein a first endpoint and an other endpoint of the usable portion of the standard sigmoid curve are determined via a second derivative of the standard sigmoid curve, and the usable portion of the standard sigmoid curve comprises a range of a plurality of points between the first endpoint and the other endpoint; and

based on a location of the observation on the standard sigmoid curve, calculating a concentration of the substance.

For example, the Application describes “a usable portion” at page 4, lines 12-13, as “the portion of the sigmoid curve between the two bounds (e.g., endpoints),” and at page 4, lines 6-11, “a first bound (e.g. endpoint) of the range is found via the second derivative of the sigmoid curve. . . [and] the other bound (e.g., endpoint) of the range is found via the second derivative of the sigmoid curve.” Claim 1 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer’s description of methods for quantifying the concentration of a nucleic acid in a nucleic acid sample does not teach or suggest at least “finding where on a usable portion of a standard sigmoid curve the observation lies, wherein a first endpoint and an other endpoint of the usable portion of the standard sigmoid curve are determined via a second derivative of the standard sigmoid curve, and the usable portion of the standard sigmoid curve comprises a range of a plurality of points between the first endpoint and the other endpoint.” Wittwer states at column 5, lines 53-64:

Upon applying a Savitzky Golay filter, each measured kinetic point is replaced by a smoothened point, calculated from a window. . . [wherein] vertical window parameters are defined as  $a/n/b$ , wherein  $a$  is the number of points taken

from the left,  $n$  is the order of the polynomial and  $b$  is the number of points taken from the right.

Wittwer also states at column 6, lines 10-11, “[f]or each smoothened kinetic point, derivatives are calculated by methods known in the art.” Thus, Wittwer does describe determining a derivative and using a filter to smoothen data. However, Wittwer does not “[find] where on a usable portion of a standard sigmoid curve the observation lies, wherein a first endpoint and an other endpoint of the usable portion of the standard sigmoid curve are determined via a second derivative of the standard sigmoid curve, and the usable portion of the standard sigmoid curve comprises a range of a plurality of points between the first endpoint and the other endpoint” because Wittwer does not determine the window parameters via a second derivative.

For at least these reasons, claim 1 and its dependent claims 2-6 are allowable over Wittwer.

***Amended independent claim 8 and dependent claims 9-10 are allowable over Wittwer***

Amended claim 8 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to calculate concentration of a substance in a test sample, the method comprising:

for a plurality of observations of a metric for the test sample, fitting a test sigmoid curve to the observations; and  
calculating a concentration of the substance in the test sample via the test sigmoid curve and a usable portion of a standard curve, wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points, wherein a first edge and a second edge of the range are determined via a second derivative of the standard sigmoid curve.

For example, the Application describes at page 4, lines 4-5, and at Figure 3 “an exemplary method 300 by which the usable portion of a sigmoid curve can be determined,” wherein a first edge of a range is defined based on a second derivative and a second edge of the range is defined based on a second derivative. Claim 8 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer’s description of methods for quantifying the concentration of a nucleic acid in a nucleic acid sample does not teach or suggest at least “calculating a concentration of the substance in the test sample via the test sigmoid curve and a usable portion of a standard curve,

wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points, wherein a first edge and a second edge of the range are determined via a second derivative of the standard sigmoid curve.” Wittwer states at column 5, lines 53-64:

Upon applying a Savitzky Golay filter, each measured kinetic point is replaced by a smoothened point, calculated from a window. . . [wherein] vertical window parameters are defined as  $a/n/b$ , wherein  $a$  is the number of points taken from the left,  $n$  is the order of the polynomial and  $b$  is the number of points taken from the right.

Wittwer also states at column 6, lines 10-11, “[f]or each smoothened kinetic point, derivatives are calculated by methods known in the art.” Thus, Wittwer does describe determining a derivative and using a filter to smoothen data. However, Wittwer does not describe “a range of a plurality of points, wherein a first edge and a second edge of the range are determined via a second derivative.” Therefore, Wittwer does not “[calculate] a concentration of the substance in the test sample via the test sigmoid curve and a usable portion of a standard curve, wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points, wherein a first edge and a second edge of the range are determined via a second derivative of the standard sigmoid curve.”

For at least these reasons, claim 8 and its dependent claims 9 and 10 are allowable over Wittwer.

***Amended independent claim 11 is allowable over Wittwer***

Amended claim 11 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to calculate concentration of a substance in a test sample, the method comprising:

finding a usable portion of a sigmoid curve, wherein first and second endpoints of the usable portion of the sigmoid curve are determined via a second derivative of the sigmoid curve, and the usable portion of the sigmoid curve comprises a range of a plurality of points between the first and second endpoints; and

calculating a concentration of the substance in the test sample via the usable portion of the sigmoid curve.

Claim 11 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of a nucleic acid in a nucleic acid sample does not teach or suggest at least "finding a usable portion of a sigmoid curve, wherein first and second endpoints of the usable portion of the sigmoid curve are determined via a second derivative of the sigmoid curve, and the usable portion of the sigmoid curve comprises a range of a plurality of points between the first and second endpoints."

Wittwer states at column 5, lines 53-64:

Upon applying a Savitzky Golay filter, each measured kinetic point is replaced by a smoothened point, calculated from a window. . . [wherein] vertical window parameters are defined as  $a/n/b$ , wherein  $a$  is the number of points taken from the left,  $n$  is the order of the polynomial and  $b$  is the number of points taken from the right.

Wittwer also states at column 6, lines 10-11, "[f]or each smoothened kinetic point, derivatives are calculated by methods known in the art." Thus, Wittwer does describe determining a derivative and using a filter to smoothen data. However, Wittwer does not describe "first and second endpoints. . . determined via a second derivative." Therefore, Wittwer does not "[find] a usable portion of a sigmoid curve, wherein first and second endpoints of the usable portion of the sigmoid curve are determined via a second derivative of the sigmoid curve, and the usable portion of the sigmoid curve comprises a range of a plurality of points between the first and second endpoints."

For at least these reasons, claim 11 is allowable over Wittwer.

***Amended independent claim 13 and dependent claims 14-17 are allowable over Wittwer***

Amended claim 13 is directed to a computer-implemented method of calculating concentration of a substance in a test sample having an unknown concentration of the substance, the method comprising:

determining a usable portion of a sigmoid curve fit to data points representing observations of a reference sample having a known concentration of the substance, wherein the usable portion of the sigmoid curve comprises a range of a plurality of points representing a range of observational values; and  
calculating the concentration of the substance in the test sample based on a subset of observations of the test sample, wherein the subset is within the range of observational values represented by the usable portion of the sigmoid curve.

For example, the Application describes at page 7, lines 13-15, “determining whether a measurement indicating concentration of live cells (e.g., the optical density) falls within a usable portion of a standard sigmoid curve representing observations taken of a sample having a known concentration of antibody.” Claim 13 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer’s description of methods for quantifying the concentration of nucleic acid in a nucleic acid sample does not teach or suggest at least “determining a usable portion of a sigmoid curve fit to data points representing observations of a reference sample having a known concentration of the substance, wherein the usable portion of the sigmoid curve comprises a range of a plurality of points representing a range of observational values; and calculating the concentration of the substance in the test sample based on a subset of observations of the test sample, wherein the subset is within the range of observational values represented by the usable portion of the sigmoid curve.” Wittwer states at column 12, lines 12-18:

As the number of bacteria increase, the absorbance increases, giving a relative measure of the number of bacteria. The second derivative maximum is calculated to give a fractional cycle number of the control sample (T).

In parallel reactions, substances A, B, and C are added to separate cuvettes with media and inoculated as before. Their growth is monitored over time as above. Curves such as shown in FIG. 6 will be obtained.

Thus, Wittwer does describe measuring absorbance, generating a curve, and calculating a fractional cycle number for a control sample T and test substances A, B, C. However, Wittwer does not determine a “usable portion of a sigmoid curve fit to data points representing observations of a reference sample having a known concentration of the substance” because Wittwer does not determine a range of a plurality of points on a curve (e.g., curve T in FIG. 6). Specifically, Wittwer does not determine a “usable portion” of a curve “wherein the usable portion. . . comprises a range of a plurality of points representing a range of observational values.” Instead, Wittwer determines a point (e.g., fractional cycle number  $C_T$ ) on a curve (e.g., curve T). A fractional cycle number is not a “range of a plurality of points representing a range of observational values.”

Furthermore, Wittwer does not “[calculate] the concentration of the substance in the test sample based on a subset of observations of the test sample, wherein the subset is within the

range of observational values represented by the usable portion of the sigmoid curve.” Wittwer states at column 12, lines 21-23, that a “magnitude and direction of the shift in fractional cycle number,” (e.g.  $C_T - C_B$ ), can indicate a “potency of inhibition.” Therefore, Wittwer does describe determining potency of inhibition based on a fractional cycle number. However, a fractional cycle number (e.g.,  $C_B$ ) is a calculated number not “a subset of observations of the test sample.” In addition, Wittwer does not describe a “subset [of observations of the test sample] within the range of observational values represented by the usable portion of the sigmoid curve.”

Therefore, Wittwer does not determine “a usable portion of a sigmoid curve fit to data points representing observations of a reference sample having a known concentration of the substance, wherein the usable portion of the sigmoid curve comprises a range of a plurality of points representing a range of observational values” and Wittwer does not calculate “the concentration of the substance in the test sample based on a subset of observations of the test sample, wherein the subset is within the range of observational values represented by the usable portion of the sigmoid curve.”

For at least these reasons, claim 13 and its dependent claims 14-17 are allowable over Wittwer.

***Amended independent claim 18 and dependent claims 20-25 are allowable over Wittwer***

Amended claim 18 is directed to a computer-implemented method of determining the concentration of antibody in a blood serum sample, the method comprising:

- receiving a measurement indicative of concentration of live cells in a test sample, wherein the test sample is generated by adding the serum to cells and a toxin neutralized by the antibody;

- determining whether the measurement falls within a usable portion of a standard sigmoid curve representing observations taken of a sample having a known concentration of antibody, wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points representing a range of observations; and

- responsive to determining the measurement falls within the usable portion, calculating a concentration via the standard sigmoid curve

Claim 18 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of nucleic acid in a nucleic acid sample does not teach or suggest at least "determining whether the measurement falls within a usable portion of a standard sigmoid curve representing observations taken of a sample having a known concentration of antibody, wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points representing a range of observations."

Wittwer states at column 12, lines 12-18:

As the number of bacteria increase, the absorbance increases, giving a relative measure of the number of bacteria. The second derivative maximum is calculated to give a fractional cycle number of the control sample (T).

In parallel reactions, substances A, B, and C are added to separate cuvettes with media and inoculated as before. Their growth is monitored over time as above. Curves such as shown in FIG. 6 will be obtained.

Wittwer also states at column 12, lines 21-23, that a "magnitude and direction of the shift in fractional cycle number," (e.g.  $C_T - C_B$ ), can indicate a "potency of inhibition." Thus, Wittwer does describe measuring absorbance, generating a curve, and calculating a fractional cycle number for a control sample T and test substances A, B, C. However, Wittwer does not describe a range of a plurality of points of a curve (e.g., a curve in FIG. 6), nor does Wittwer determine a "usable portion" of a curve "wherein the usable portion . . . comprises a range of a plurality of points representing a range of observations." Instead, Wittwer determines a point (e.g., fractional cycle number  $C_T$ ) on a curve (e.g., curve T). A fractional cycle number is not a "range of a plurality of points," nor is a fractional cycle number "a measurement."

Therefore, Wittwer does not determine "whether the measurement falls within a usable portion of a standard sigmoid curve representing observations taken of a sample having a known concentration of antibody, wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points representing a range of observations" and Wittwer does not calculate the concentration responsive to the determination.

For at least these reasons, claim 18 and its dependent claims 20-25 are allowable over Wittwer.



***Amended independent claim 19 is allowable over Wittwer***

Claim 19 has been amended to recite the features of claim 18 in independent form. Amended independent claim 19 is therefore allowable over Wittwer for at least the same reasons stated above with respect to claim 18.

***Amended independent claim 26 and dependent claims 27-29 are allowable over Wittwer***

Amended claim 26 is directed to a software system encoded on one or more computer-readable media, the software system comprising:

- a representation of a characteristic sigmoid curve;
- means for designating a usable portion of the characteristic sigmoid curve, wherein first and last endpoints of the usable portion of the characteristic sigmoid curve are determined via a second derivative and wherein the usable portion comprises a range of a plurality of points between the first and last endpoints;
- means for receiving at least one observation of a test sample;
- means for determining whether the observation of the test sample is within the usable portion of the characteristic sigmoid curve; and
- means for calculating a concentration for the observation responsive to determining that the observation is within the usable portion of the characteristic sigmoid curve.

Claim 26 stands rejected over Wittwer. However, Wittwer does not teach or suggest each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of nucleic acid in a nucleic acid sample does not teach or suggest at least "means for designating a usable portion of the characteristic sigmoid curve, wherein first and last endpoints of the usable portion of the characteristic sigmoid curve are determined via a second derivative and wherein the usable portion comprises a range of a plurality of points between the first and last endpoints." Wittwer states at column 5, lines 53-64:

Upon applying a Savitzky Golay filter, each measured kinetic point is replaced by a smoothened point, calculated from a window. . . [wherein] vertical window parameters are defined as  $a/n/b$ , wherein  $a$  is the number of points taken from the left,  $n$  is the order of the polynomial and  $b$  is the number of points taken from the right.

Wittwer also states at column 6, lines 10-11 "[f]or each smoothened kinetic point, derivatives are calculated by methods known in the art." Thus, Wittwer does describe determining a derivative

and using a filter to smoothen data. However, Wittwer does not describe “first and last endpoints. . . determined via a second derivative.” Therefore, Wittwer does not describe “designating a usable portion of the characteristic sigmoid curve, wherein first and last endpoints of the usable portion of the characteristic sigmoid curve are determined via a second derivative and wherein the usable portion comprises a range of a plurality of points between the first and last endpoints.”

For at least these reasons, claim 26 and its dependent claims 27-29 are allowable over Wittwer.

***Independent claim 30 is allowable over Wittwer***

Claim 30 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to indicate presence of a substance in a test sample, the method comprising:

for at least one observation of a metric for the test sample, determining whether the observation is higher than a threshold value, wherein the threshold value is determined via a first derivative of a standard sigmoid curve; and responsive to determining the observation is higher than the threshold value, indicating presence of the substance.

Claim 30 stands rejected over Wittwer. However, Wittwer does not teach each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of nucleic acid in a nucleic acid sample does not teach or suggest at least “for at least one observation of a metric for the test sample, determining whether the observation is higher than a threshold value, wherein the threshold value is determined via a first derivative of a standard sigmoid curve; and responsive to determining the observation is higher than the threshold value, indicating presence of the substance.” The Action relies on the following description in Wittwer column 5, lines 9-25:

In yet another aspect of the invention, the principle of calculating derivatives in order to generate quantitative data can be applied to the analysis of growth rates of microorganisms or cell populations (see Example 3 ). Accordingly, the present invention is also directed to a method for analyzing the effect of a compound on the growth rate of a microorganism or a cell population, comprising

- a) growing said microorganism or cell population in presence of the compound,
- b) determining the cell number of said microorganism or cell population as a function of growth time,
- c) calculating the first, second, or  $n$ th order derivative of said function, wherein  $n$  is a natural number, and
- d) determining the maximum, zero value or minimum of said derivative as a measure of the effect of said compound.

Wittwer also states at column 5, line 67 to column 6, line 2, that “[d]etermination of such extrema provides suitable set points for the definition of an unique and reliable fractional cycle number characteristic for each kinetic value.” Thus, Wittwer does describe determining “quantitative data [that] can be applied to the analysis of growth rates” (e.g., a fractional cycle number) from extrema of a derivative. However, Wittwer does not describe a threshold value. Further, Wittwer does not describe “indicating presence of the substance” responsive to “determining the observation is higher than the threshold value.”

For at least these reasons, claim 30 is allowable over Wittwer.

***Rejections under 35 U.S.C. § 103(a) over Wittwer in view of Kaastrup***

The Action rejects claims 7, 12 and 23 under 35 U.S.C. § 103(a) over Wittwer in view of U.S. Pat. Publication No. 2002/0160012 to Kaastrup (Kaastrup). Applicant respectfully traverses this rejection.

Claim 7 depends from claim 1 and is directed to one or more computer-readable media comprising computer-executable instructions for performing a method to calculate concentration of a substance in a test sample, the method comprising:

- for at least one observation of a metric for the test sample, finding where on a usable portion of a standard sigmoid curve the observation lies, wherein first and last endpoints of the usable portion of the standard sigmoid curve are determined via a second derivative of the standard sigmoid curve, and the usable portion of the standard sigmoid curve comprises a range of a plurality of points between the first and last endpoints; and

- based on a location of the observation on the standard sigmoid curve, calculating a concentration of the substance in the test sample, wherein the observation indicates optical density for the test sample, wherein the concentration indicates an amount of antibody in the test sample, and

wherein the concentration indicates an amount of anti-PA IgG in the test sample.

Claim 7 stands rejected over Wittwer in view of Kaastrup. However, neither Wittwer alone nor Wittwer in combination with Kaastrup teaches or suggests each and every element of the claim.

Applicant has already stated reasons for the allowance of claim 1 (from which claim 7 depends) over Wittwer. Kaastrup is directed to a vaccine chip technology that exploits the immunostimulating effects of a fragment of TGF $\beta$  for immunization and other medical treatments. Kaastrup is silent concerning calculating derivatives and on determining "a usable portion" of a curve. Kaastrup does not cure the deficiencies of Wittwer.

For at least these reasons, claim 7 is allowable over Wittwer alone or in view of Kaastrup.

Amended claim 12 is directed to one or more computer-readable media comprising computer-executable instructions for performing a method comprising:

for a plurality of dilutions of a test sample, receiving respective measurements of optical density indicating concentration of live cells within the dilutions;

via the measurements, calculating a concentration of anti-PA IgG for the test sample via a usable portion of a sigmoid curve representing concentrations of live cells within dilutions of a reference sample having a known quantity of anti-PA IgG, wherein the sigmoid curve is represented via a four-parameter logistic technique, and wherein a usable portion of the sigmoid curve comprises a range of a plurality of points between two bounds determined via a second derivative of the sigmoid curve; and

indicating the concentration of anti-PA IgG for the test sample.

Claim 12 stands rejected over Wittwer in view of Kaastrup. However, neither Wittwer alone nor Wittwer in combination with Kaastrup teaches or suggests each and every element of the claim.

Wittwer's description of methods for quantifying the concentration of a nucleic acid in a nucleic acid sample does not teach or suggest at least "calculating a concentration of anti-PA IgG for the test sample via a usable portion of a sigmoid curve representing concentrations of live cells within dilutions of a reference sample having a known quantity of anti-PA IgG, wherein the sigmoid curve is represented via a four-parameter logistic technique, and wherein a usable portion of the sigmoid curve comprises a range of a plurality of points between two bounds determined via a second derivative of the sigmoid curve." Wittwer states at column 5, lines 53-64:

Upon applying a Savitzky Golay filter, each measured kinetic point is replaced by a smoothened point, calculated from a window. . . [wherein] vertical window parameters are defined as  $a/n/b$ , wherein  $a$  is the number of points taken from the left,  $n$  is the order of the polynomial and  $b$  is the number of points taken from the right.

Wittwer also states at column 6, lines 10-11, “[f]or each smoothened kinetic point, derivatives are calculated by methods known in the art.” Thus, Wittwer does describe determining a derivative and using a filter to smoothen data. However, Wittwer does not describe “a range of a plurality of points between two bounds determined via a second derivative of the sigmoid curve.” Therefore, Wittwer does not “[calculate] a concentration of anti-PA IgG for the test sample via a usable portion of a sigmoid curve representing concentrations of live cells within dilutions of a reference sample having a known quantity of anti-PA IgG, wherein the sigmoid curve is represented via a four-parameter logistic technique, and wherein a usable portion of the sigmoid curve comprises a range of a plurality of points between two bounds determined via a second derivative of the sigmoid curve.”

Kaastrup is directed to a vaccine chip technology that exploits the immunostimulating effects of a fragment of TGF $\beta$  for immunization and other medical treatments. Kaastrup does not cure the deficiencies of Wittwer.

For at least these reasons, claim 12 is allowable over Wittwer alone or in view of Kaastrup.

Claim 23 depends from claim 18 and is directed to a computer-implemented method, encoded on a computer-readable medium, of determining the concentration of antibody in a blood serum sample, the method comprising:

- receiving a measurement indicative of concentration of live cells in a test sample, wherein the test sample is generated by adding the serum to cells and a toxin neutralized by the antibody;

- determining whether the measurement falls within a usable portion of a standard sigmoid curve representing observations taken of a sample having a known concentration of antibody, wherein the usable portion of the standard sigmoid curve comprises a range of a plurality of points representing a range of observations; and

- responsive to determining the measurement falls within the usable portion, calculating a concentration via the standard sigmoid curve, wherein the antibody is anti-PA IgG.

Claim 23 stands rejected over Wittwer in view of Kaastrup. However, neither Wittwer alone nor Wittwer in combination with Kaastrup teaches or suggests each and every element of the claim.

Applicant has already stated reasons for the allowance of claim 18 (from which claim 23 depends) over Wittwer. Kaastrup is directed to a vaccine chip technology that exploits the immunostimulating effects of a fragment of TGF $\beta$  for immunization and other medical treatments. Kaastrup does not cure the deficiencies of Wittwer.

For at least these reasons, claim 23 is allowable over Wittwer alone or in view of Kaastrup.

#### ***Computer-readable media***

The Action argues that the claims are obvious because it has been held that broadly providing a mechanical or automatic means to replace manual activity involves only routine skill in the art. Applicant disagrees that the recited arrangements are mere replicates of manual activity. Further, as pointed out above, there are elements missing from the cited art. Accordingly, the claims are allowable at this time.

#### ***Request for Interview***

If any issues remain, the Examiner is formally requested to contact the undersigned attorney prior to issuance of the next Office Action in order to arrange a telephonic interview. It is believed that a brief discussion of the merits of the present application may expedite prosecution. Applicant submits the foregoing formal Amendment so that the Examiner may fully evaluate Applicant's position, thereby enabling the interview to be more focused.

This request is being submitted under MPEP § 713.01, which indicates that an interview may be arranged in advance by written request.

**Conclusion**

The claims in their present form should now be allowable. Such action is respectfully requested.

Respectfully submitted,

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